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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,264	09/25/2003	Sen-Itiroh Hakomori	020805-15210100	3225

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/669,264	HAKOMORI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *2,4,5 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/19/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *080604 & 070907*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 09/25/03 and 07/09/07.

Election

2) Acknowledgment is made of Applicants' election of species filed 01/30/08 in response to the election of species requirement mailed 12/31/07. Applicants have elected the lactone carbohydrate antigen mimetic species. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P § 818.03(a)).

Status of Claims

3) New claims 3-12 have been added via the amendment filed 07/09/07.

Claims 1-12 are pending.

Claims 2, 4, 5 and 12 have been withdrawn from consideration as being directed to a non-elected species. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 1, 3 and 6-11 are under examination.

Information Disclosure Statements

4) Acknowledgment is made of Applicants' Information Disclosure Statements filed 08/06/04 and 07/09/07. The information referred to therein has been considered and an initialed copy is attached to this Office Action.

Sequence Listing

5) Acknowledgment is made of Applicants' submission of Sequence Listing, which has been entered on 02/06/07.

Priority

6) The instant application is a continuation of application SN 10/040,336 filed 01/09/2002, now abandoned, which is a continuation of application SN 09/696,213 filed 10/26/00, now

abandoned, which is a continuation of application SN 09/253,024, filed 02/19/99, now abandoned.

Objection(s) to Specification

7) The specification is objected to for the following reasons:

(a) The first paragraph of the specification does not provide information on the status of the earlier US applications as indicated above under the section 'Priority'. Amendment to the specification is needed.

(b) The amino acid sequences recited on pages 17, 19 and 20 and in Figure 9B of the specification contain more than four amino acids, yet are not identified by a SEQ ID NO as required under 37 C.F.R 1.821 through 1.825. Any sequences recited in the instant specification which are encompassed by the definitions for nucleotide and/or amino acid sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2) must comply with the requirements of 37 C.F.R 1.821 through 1.825. Note that branched sequences are specifically excluded from this definition.

APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R 1.821(g).

(c) On page 22, line 22, the address of the American Type Culture Collection is incorrect. Effective 23 March 1998, ATCC has a new address: 10801 University Boulevard, Manassas, VA 20110-2209. Amendment to the specification is suggested to reflect this. It is suggested that Applicants examine the whole specification to make similar correction to the address, wherever it appears.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

8) New claim 10 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 10 includes the limitation: 'an inhibitor of suppressor T cells'. However, there is no descriptive support in the specification for this limitation. While lines 20-22 of page 15 of

the specification are supportive of 'an inhibitor of suppressor T-cell response', there is no support for 'an inhibitor of suppressor T cells'. The limitations 'T cells' and 'T cell response' are different from one another in terms of meaning and scope. Furthermore, while there is support for the cyclophosphamide species, there is no descriptive for the generic limitation 'an inhibitor of suppressor T-cells' which includes within its scope many such inhibitor species other than the single disclosed cyclophosphamide species. Therefore, the above-identified limitations in the instant new claim are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after 608.04(c).

Applicants are invited to point to specific line and page numbers of the specification, as originally filed, that provide descriptive support for the limitations identified above, or alternatively, remove the new matter from the claim. Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

9) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

10) Claims 6-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 6 is indefinite and/or confusing in the limitation: 'vaccine of claim 1, comprising a multivalent antigen'. Claim 6 depends from claim 1, wherein the recited antigen is limited to a carbohydrate antigen. Is 'a multivalent antigen' recited in claim 6 different from the carbohydrate antigen recited in the base claim 1?

(b) Claims 7-8 are indefinite and/or confusing in the limitation: 'elicits an IgG response'; 'elicits an IgM response'; and 'elicits a T cell response' respectively, because it is unclear what this response is specific to. Is this response directed to the carbohydrate antigen, mimetic of the carbohydrate antigen, or the cancer cells?

Rejection(s) under 35 U.S.C. § 102

11) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12) Claims 1-3, 7, 9 and 11 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hakomori (US 5,308,614).

It is noted that Example 3 of the instant application describes GM3 lactones. It is further noted that the instant specification at the top of page 7 discloses that Tn and sialyl Tn are common on all types of mucin glycoproteins irrespective of human and various animal species.

Hakomori disclosed a vaccine for active immunization against tumors comprising a pharmaceutically acceptable carrier and a strongly immunogenic GM3 ganglioside lactone which induced DH2 IgG3 antibody that suppressed the growth of ganglioside-containing melanoma tumors *in vitro* and *in vivo*. The vaccine contained saline, PBS, Ringers' solution, or *Salmonella minnesota* adjuvant. See abstract; title; Field of the Invention; Figures 1B and 4-6; Summary of the Invention; Detailed Description of the Invention; Examples 1, 2 and 4; and Tables I and VI. That an IgG response is indicative of a T cell response is inherent from the teachings of Hakomori in light of what is well known in the art. For example, see second full paragraph in column 11 of Lopez *et al.*

Claims 1-3, 7, 9 and 11 are anticipated by Hakomori. The reference of Lopez *et al.* is not used as a secondary reference in combination with Hakomori, but rather is used to show that every element of the claimed subject matter is disclosed by Hakomori with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978).

13) Claims 1-3, 7, 9 and 11 are rejected under 35 U.S.C. § 102(b) as being anticipated by Dohi *et al.* (*Cancer Res.* 48: 5680-5685, 1988) as evidenced by Lopez *et al.* (US 5,817,513).

It is noted that Example 3 of the instant application describes GM3 lactones. It is further

noted that the instant specification at the top of page 7 discloses that Tn and sialyl Tn are common on all types of mucin glycoproteins irrespective of human and various animal species.

Dohi *et al.* taught an antitumor vaccine comprising highly immunogenic lactone of tumor-associated ganglioside GM3 antigen, PBS (i.e., pharmaceutically acceptable carrier) and *S. minnesotae* adjuvant. The vaccine is for use in prevention of tumor cell growth *in vivo*. The vaccine induced an anti-GM3 and anti-GM3 lactone IgG3 antibody response which showed inhibition of growth of melanoma cells *in vitro* and *in vivo*. See abstract; last full paragraph on page 5680; paragraph bridging the two columns on page 5680; and Figure 1. That an IgG response is indicative of a T cell response is inherent from the teachings of Dohi *et al.* in light of what is well known in the art. For example, see second full paragraph in column 11 of Lopez *et al.*

Claims 1-3, 7, 9 and 11 are anticipated by Dohi *et al.* The reference of Lopez *et al.* is not used as a secondary reference in combination with the reference of Dohi *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Dohi *et al.* with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978).

14) Claims 1, 3, 9 and 11 are rejected under 35 U.S.C. § 102(b) as being anticipated by Harada *et al.* (*Jpn. J. Cancer Res.* 81: 383-387, 1990).

Harada *et al.* taught a vaccine composition comprising GM3-lactone liposomes that induced anti-melanoma T cell responses in mice by inducing anti-melanoma cytotoxic T cells (CTL) and suppressor T cells. The vaccine comprises the GM3-lactone, PBS (i.e., pharmaceutically acceptable carrier) and dipalmytoylphosphatidylcholine, cholesterol and diacetylphosphate (i.e., adjuvant). See abstract; Materials and Methods; Figure 1; and Results.

Claims 1, 3, 9 and 11 are anticipated by Harada *et al.*

15) Claims 1, 3 and 8 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kawashima *et al.* (*Int. J. Cancer* 58: 263-268, 1994).

Kawashima *et al.* taught a vaccine comprising PBS and a purified GM3 lactone (GM3-L), GM1 lactone, and GD1a lactone adsorbed to *S. minnesota* for use in immunization. The vaccine induced IgM antibodies. See abstract; Materials and Methods; Results; Figures 1 and 6;

and Table I.

Claims 1, 3 and 8 are rejected under 35 U.S.C. § 102(a) as being anticipated by Kawashima *et al.*

Rejection(s) under 35 U.S.C. § 103

16) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

17) Claim 10 is rejected under 35 U.S.C. § 103(a) as being anticipated by Hakomori (US 5,308,614) or Dohi *et al.* (*Cancer Res.* 48: 5680-5685, 1988) as applied to claim 1 above, and further in view of Hoon *et al.* (*Cancer Res.* 50: 5358-5364, 1990).

It is noted that the instant specification identifies cyclophosphamide as an inhibitor of suppressor T-cell response. See lines 20-22 of page 15.

The teachings of Hakomori or Dohi *et al.* are explained above which do not expressly teach the presence of an inhibitor of suppressor T cells in their vaccine.

However, Hoon *et al.* showed the routine addition in the art to melanoma cancer vaccines the biological response modifier cyclophosphamide, which is an immunomodulator of suppressor T-cell function. See abstract and page 5358.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Hoon's biological response modifier cyclophosphamide, to Hakomori's or Dohi's antitumor vaccine to produce the instant invention with a reasonable

expectation of success. Given the routine addition of cyclophosphamide to an art-known anticancer vaccine, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of advantageously providing Hakomori's or Dohi's antitumor vaccine with a biological response modifier which is an immunomodulator of suppressor T-cell function as taught by Hoon *et al*.

Claim 10 is *prima facie* obvious over the prior art of record.

Remarks

18) Claims 1, 3 and 6-11 stand rejected.

19) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

20) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

21) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Shanon Foley, can be reached on (571) 272-0898.

/S. Devi/
S. Devi, Ph.D.
Primary Examiner, AU 1645

April, 2008